July 8, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11220-original article).

Title: Acupuncture at heterotopic acupoints enhances jejunal motility in constipated and diarrhoeic rats
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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11220

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated according to the format of Original article you emailed me

2 Revision has been made according to the suggestions of the reviewer

(1) Critique? Abstract is not in the usual style of background, methods, results, discussion and conclusion?
Answer: Thanks for the reviewer's reminder. We rewrote the abstract according the format of original article the editor emailed us and have replaced the old one with it in the revised manuscript.

(2) Transit time was not measured, only changes in the intraluminal pressures and contraction frequencies (which I assume is "motility frequencies").
Answer: Yes, you are right. We did not measure the transit time. Here we used inbuilt balloon pressure detection system to detect jejunal motility. The recorded waves contain peristalsis and translator waves. In this study, the peristalsis waves, as the waves of muscular contractions, had high frequency and low amplitude, and were used to evaluate the effect of acupuncture on jejunal motility, because it showed more stable in amplitude and duration than the translatory waves. The changes in the peristalsis waves were caused by muscular contractions and could be measured through an intraluminal pressure or frequency.

(3) Results ? Peristalsis waves were made up of changes in intraluminal pressure and frequency of waves?
Answer: The peristalsis waves stand for muscle contraction that propel contents from one point to another, and have high frequency and low amplitude, therefore the changes could happen in amplitude which is represented by intrajejunal pressure, or frequency.

(4) The heterotopic acupuncture points increased intraluminal pressures in normal, constipated and diarrhea. Rats where the homotopic acupuncture point reduced pressure and mobility waves. It is difficult to conceive that this is increased small bowel (jejunal) motility since frequency of contraction (frequency of waves) did not change. One could attribute this to increased segmentation or tonic small bowel contraction even when applying an anti-muscarinic only ST37 increased wave frequency (by 10%) amplitude of contraction was increased to a much greater extent than frequency.
Answer: A great number of reports provided evidence that inbuilt balloon pressure detection system is an effective approach to evaluate gastrointestinal motility [1-10], although it doesn't like electrointestinogram which can show the muscle contraction directly. The gastrointestinal motility reflects the organic function as a

result of myoelectric activation, whereas not each myoelectric activation recorded produces gastrointestinal motility. Generally, changes of gastrointestinal motility could happen in amplitude or frequency. Here we focus our interest in the functional regulation of acupuncture. In the current study, the frequency of the circular muscle contraction was not changed significantly before and after treatment with acupuncture at heterotopic or homotopic acupoint, but the amplitude of the circular muscle contraction was changed significantly, suggesting that acupuncture could regulate jejunal motility.

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(5) The increased intraluminal pressures could be due to release of enteric endogenous opioids. This is plausible since frequency of contraction is unchanged. Opioids would cause contraction of circular muscle (increasing intraluminal pressures) without peristalsis (inhibits longitudinal muscle)?

Answer: Here we would like to greatly appreciate the reviewer's suggestion that the increase intrajejunal pressure could be induced by the release of enteric endogenous opioids. In the future study, we will identify whether acupuncture at heterotopic acupoints can cause the release of enteric endogenous opioids and elucidate whether opioids play an important role in the regulation of gastrointestinal motility by acupuncture.

(6) To my estimation, the authors were measuring intraluminal pressures and contraction of small bowel without measuring meaningful transit since motility was not measured and frequency of contraction unchanged. Demonstrating that a marker passes through the small bowel at a more rapid rate (reduced time) under heterotopic acupuncture would be more convincing?

Answer: Honestly, it is a good idea to detect the time that a marker passes through the small bowel and then evaluate the effect of heterotopic acupuncture on the jejunal motility, however, a challenge will be raised: acupuncture at the acupoints which were used in this study can affect not only jejunum, but also gastric and colon. In future study, we will try it through combining with CT or PET.

(7) Page 17, last paragraph jejunal is misspelled?
Answer: Thanks. Jejunal is correct. However there are wrong spellings in the last first and second paragraph. We already corrected it.

(8) It is a well-written manuscript.
Answer: We thank you for your evaluation.

(9) Statistics are adequate and rather standard for animal studies. The authors may want to directly state the primary outcomes and method of analysis for primary outcomes rather than practicing them in separate paragraphs.
Answer: We thank the reviewer for the suggestion, and already merged the paragraphs together.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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